# MALE GENITOURINARY TUBERCULOSIS -13 YEARS EXPERIENCE AT A TERTIARY CARE CENTER IN INDIA

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**Abstract.** We conducted a retrospective study of genitourinary tuberculosis (TB) among males attending a hospital in the northern Himalayan region of India. Records from 1 January 1997 to 31 December 2009 were reviewed for clinical history, relevant radiological findings laboratory data, histopathology and treatment. Of the 1,113 male urogenital non-neoplastic specimens received at the histopathology laboratory of the hospital, tuberculosis was diagnosed in 25 cases (2.2%). Urinary bladder and prostate were the most common organs involved. Thirty-six percent of cases had a previous history of TB; 12% of cases presented with no symptoms. Ziehl-Neelsen staining was positive in 72% of cases. Cultures were positive for TB in 42.8% of cases and polymerase chain reaction was positive in two cases in which it was performed. Antituberculosis treatment was required for up to 12 months in some cases and surgery was required in 32% of cases. Genitourinary TB in this study had varying presentations. Cases having strong clinical and radiological findings and suggestive histopathology for tuberculosis, even without demonstration of mycobacteria may be considered for TB treatment, particularly in endemic areas. Patients living in more remote areas may have more specific and severe symptoms due to late presentation. Histopathology plays a crucial role in diagnosis due to lack of sophisticated techniques. The emphasis should be on early detection followed by prompt treatment to avoid further complications.

**Keywords:** genitourinary tuberculosis, prostate, kidney, diagnosis, India

## INTRODUCTION

Tuberculosis (TB) is a major public health problem in developing and developed countries. The recent surge in reported cases of TB is mainly attributable to Human Immunodeficiency Virus (HIV) infection, emergence of resistant bacilli and human migration (Shafer and Edlin, 1996; Wise, 2009). Pulmonary TB comprises 68.4% of cases and extrapulmonary TB comprises 20-25% of cases (Alan *et al*, 2006). Genitourinary tuberculosis (GUTB) is one of the most common forms of extrapulmonary TB comprising 27% of extrapulmonary TB cases worldwide (Das *et al*, 2008). GUTB is a serious disease in India, but the burden of GUTB in Uttarakhand State, located mostly in the northern Himalayas of India, has been little studied.

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Table 1
Occupation and location of male patients with urogenital tuberculosis.

| Location and occupation | No. of cases (%) |
|---|---|
| Hilly region of state | |
| Farmers | 8 (32) |
| Laborers | 5 (20) |
| Students | 2 (8) |
| Unknown | 2 (8) |
| Non-hilly region of state | |
| Farmers | 6 (24) |
| Local business persons (shopkeeper) | 2 (8) |

We conducted a study to determine the frequency, clinical presentation, diagnostic modalities used, including laboratory and radiological investigations, and management of GUTB among males in this region by reviewing records from a 13 year period to provide information to help develop measures for early diagnosis and management of this disease.

## MATERIALS AND METHODS

We retrospectively reviewed all the cases and hispopathology of male patients with GUTB who presented to the hospital from 1 January 1997 to 31 December 2009. The clinical history, relevant radiological, laboratory and histopathology findings and treatment were reviewed. The occupation and socioeconomic status of each patient were recored.

## RESULTS

Of 1,113 male urogenital histopathology specimens received at the Department of Pathology for non-neoplastic diseases during the study period, GUTB was diagnosed in 25 cases. Table 1 shows the locations and occupations of these 25 GUTB patients. Thirty-two percent of patients from the hilly region and 24% of patients from non-hilly region of the state were farmers. The culture results showed no evidence of bovine tuberculosis in these cases. Eighty percent of patients lived with a combined family and had a low socioeconomic status, with an average family size of more than 6 people.

Table 2 shows the different male urogenital organs involved by the TB, along with the frequencies and percentages of involvement. The urinary bladder was the most common organ involved followed by the prostate. No cases of penile and urethral TB were found.

Table 3 shows the different clinical features of the patients with GUTB. The mean age of presentation was 37.7 years. Thirty-six percent had a previous history of TB and 12% had no symptoms. Seven patients (28%) were alcoholics and of these, 3 patients had alcoholic liver disease. Three patients with GUTB (12%) had a history of diabetes.

Table 4 shows the various radiological findings among the GUTB cases. Gross pathology findings among cases included diffuse spotty calcifications with necrosis; kidneys had scars and deformities of the calyces. Microscopic examination with hematoxylineosin staining showed epithelioid cell granulomas, Langhan's giant cells and varying amounts of caseous necrosis with inflammatory cells. Ziehl-Neelsen (ZN) staining was positive for acid-fast bacilli (AFB) in 18 cases (72%) and the other seven cases were histopathologically reported as suggestive of TB. Culture of the urine was positive for TB in 42.8% of cases. A polymerase chain reaction (PCR) test was positive for TB in the two cases in

Table 2
Frequency of tuberculosis in different male urogenital organs.

| Organ | Frequency (%) |
|---|---|
| Kidney | 2 (12) |
| Ureter | 2 (8) |
| Urinary bladder | 7 (28) |
| Urethra | 0 (0) |
| Prostate | 6 (24) |
| Epididymis | 3 (12) |
| Testes | 3 (12) |
| Scrotum | 1 (4) |
| Penis | 0 (0) |
| Total | 25 (100) |

Table 3
Clinical features in male patients with urogenital tuberculosis.

| | |
|---|---|
| Mean age (years) | 37.7 |
| Lumbar pain (%) | 56 |
| Urgency and increased frequency of micturation (%) | 56 |
| Dysuria (%) | 52 |
| Hematuria (%) | 44 |
| Pyuria (%) | 40 |
| Previous history of tuberculosis (%) | 36 |
| Fever and malaise (%) | 32 |
| No symptoms (%) | 12 |
| Infertility (%) | 12 |
| Renal failure (%) | 8 |
| Recurrent abscess (%) | 8 |
| Scrotal lump (%) | 8 |
| Scrotal sinus (%) | 4 |

which it was performed. Semen examination was done in nine cases which showed low semen volumes, oligospermia, leukospermia or decreased motility. An enzyme linked immunosorbent assay (ELISA) for HIV was negative in the eight cases in which it was performed. One prostate had a recurrent acute abscess with symptoms of acute bacterial infection resistant to antibiotics. The prostatic biopsy revealed AFB on ZN staining confirming TB.

All the cases were treated with antitubercular treatment (ATT) comprised of isoniazid, rifampicin, and pyrizinamide with or without ethambutol for the initial two to three months. After this isoniazid and rifampicin were continued for another six to nine months depending on the severity of the disease, response and compliance of the patient. Three cases were given empirical ATT based on the finding of a granuloma and necrosis on biopsy, but with a negative culture, the absence of AFB on biopsy and negative urine for AFB with ZN staining. ATT was effective in most cases; surgical intervention was required in eight cases. Abscess drainage was done in four cases, urethral dilation for stenosis was performed in one case, unilateral nephrectomy was performed in one case and bladder augmentation due to a contracted fibrosed bladder was conducted in two cases. All cases responded adequately to treatment.

## DISCUSSION

TB is an important cause of morbidity and mortality in India, especially with the emergence of treatment resistant bacilli and HIV infections (Chakraborty, 2004). GUTB, a common type of extrapulmonary TB, can have a variable presentation; the severity of the disease is related to the time of diagnosis (Figueiredo and Lucon, 2008). Human infection is mainly caused by *Mycobacterium tuberculosis* and *M. bovis*. Immunity is predominantly mediated by T-helper cells, cytokines and the genetic make up of the host (McAdam and Sharpe, 2006). GUTB may occur as a secondary infection due to decreased

Table 4
Radiological findings in male patients with urogenital tuberculosis.

| Radiological findings | No. of cases |
|---|---|
| Multiple stenoses in genitourinary tract | 8 |
| Calyceal dilatation and irregularities | 7 |
| Non-functioning kidney | 2 |
| C.T. scan revealed a well defined round to oval rim enhancing hypodense lesion in the prostate | 2 |
| Ultrasound showed well defined rounded hypoechoic lesions in the prostate and epididymis | 4 |

cellular immunity (Das *et al*, 2008). Immunosuppression may be due to malnutrition, acquired immunodeficiency or extreme age. Possible modes of spread to the genitourinary organs included direct extension, hematogenous spread and descending infection (Eastwood *et al*, 2001; Das *et al*, 2008). Testicular involvement by hematogenous spread and venereal transmission is rare (Das *et al*, 2008). A high index of suspicion should be maintained in patients with HIV infection, post-transplant patients, children with nephrotic syndrome and cases of vitamin D deficiency (Gulati *et al*, 1997; Wilkinson *et al*, 2000; Thomas, 2002). In the present study no such cases were observed, but 36% of cases had a previous history of TB, revealing previous history of TB is an important risk factor for GUTB. This risk is similar in both developing and developed countries (Figueiredo and Lucon, 2008). In contrast to other studies where the kidneys, epididymis or testes were the most commonly involved organs in GUTB, the present study showed the urinary bladder was most commonly involved followed by the prostate (Kulchavenya and Khomyakov, 2006; Wise and Shteynshlyuger, 2008). Scrotal and testicular TB was rarely seen in the present study and there were no cases of penile or urethral tuberculosis. Penile and urethral TB are rare, with urethral TB occurring in 1.9-4.5% of all cases of GUTB; penile TB rarely develops after sexual contact (Figueiredo and Lucon, 2008). Urethral TB is rare despite the constant exposure to infected urine. In the present study, epididymal and scrotal TB were observed in younger age groups than TB in other genitourinary organs. We found most patients presented with features related to genitourinary organs; few had symptoms of renal failure or infertility. Some patients presented with no symptoms; a possible reason for this may be late presentation of these patients to the hospital from remote areas of the Himalayan region, leading to more specific and severe symptoms in addition to a delayed diagnosis. Figueiredo and Lucon (2008) concluded cases of GUTB from developed countries usually have less severe presentations and specific symptoms along with less delay in diagnosis compared to developing countries.

Germ cell tumor is important in the differential diagnosis of testicular TB. In the present study diagnosis was confirmed by biopsy, thus highlighting the importance of histopathology for diagnosis. Heaton *et al* (1989) concluded

testicular tumors were an important part of the differential diagnosis of testicular TB; early biopsy may be helpful to confirm the diagnosis. One case in our study was a man with prostatic TB who presented with multiple recurrent prostate abscesses resistant to antibiotics; the diagnosis was confirmed by demonstration of AFB on biopsy. This type of presentation is usually seen in patient with AIDS (Trauzzi *et al*, 1994). However, this patient was HIV negative. Prostatic TB can have varying presentations and biopsy is the gold standard for diagnosis. Although hemospermia has been reported to raise a suspicion of prostatic or seminal vesicle TB, in the present study no hemospermia was observed (Pal, 2002). It has been reported intravenous urography shows radiological abnormalities suggestive of GUTB in 88.1% of clinically suspected cases (Hemal *et al*, 2000). Multiple strictures of urinary system were the most common finding observed on radiological examination, consistent with other studies, and is most suggestive of GUTB (Wang *et al*, 2003).

The various modalities for diagnosing GUTB include histopathological examination, culture, demonstration of AFB by ZN staining and nucleic acid amplification by PCR. An important feature of the present study was the demonstration of AFB on histopathological examination in nearly 71% of cases; other studies have reported the sensitivity of detecting AFB on histology can be as low as 40-50% (Das *et al*, 2008). This may be due to the meticulous search by the pathologist for AFB on ZN staining of histopathological specimens. This shows ZN staining is an important diagnostic tool in areas where other advanced modalities like PCR are unavailable. An advantage of the PCR test for TB is it provides rapid detection with high sensitivity (95.6%) and specificity (98.1%) for the diagnosis of TB even in the presence of a few bacilli (Moussa *et al*, 2000).

This study also highlights the fact that cases without AFB on histopathology or culture but demonstrating epithelioid cell granulomas and/or caseous necrosis on histopathology along with a clinicoradiological consistent with tuberculosis are suitable for empiric antitubercular treatment in developing countries. ATT with isoniazid, rifampicin and pyrizinamide with or without ethambutol for eight to twelve months was considered adequate for the treatment of these patients. Although other studies have recommended shorter courses of four to six months of chemotherapy the present study found longer duration was required for adequate treatment of GUTB (Cek *et al*, 2005). Malnutrition, poor compliance, poor socioeconomic status and severity of disease may be reasons why longer duration of treatment was needed.

Surgery was required in 32% of cases in the present study, showing delayed diagnosis leads to more destruction of organs requiring surgical intervention. The efficacy of chemotherapy may be monitored by histological follow-up (Gupta *et al*, 2008).

In conclusion, GUTB can have varying clinical presentations; therefore, cases with a strong clinicoradiological and histopathological findings suggestive of TB, even without the demonstration of AFB of stain or a positive culture, may be suitable for ATT, particularly in developing countries where tuberculosis is endemic. Patients living in remote regions may have symptoms more specific for GUTB due to their late presentation. Histopathology plays a crucial role in the diagnosis of GUTB, although more advanced molecular diagnostic techniques, like PCR, may be required in cases where

other diagnostic modalities fail. However, due to financial constraints and limited facilities, the demonstration of AFB on biopsy remains the most useful method for confirming GUTB. Emphasis should be placed on early detection of cases followed by prompt treatment to avoid further complications.

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